Research Paper

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A Study on Immune Response of Hepatitis B Vaccine Among Medical Interns

Medical Science

KEYWORDS : Hepatitis B virus, Anti HBs titer, Immune response, Medical interns, Booster dos

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ABSTRACT

Hepatitis B is the most important infectious occupational hazard which Indian medical students encounter. As the universal precaution is not effectively followed among medical students, studies are needed to document the compliance to and effectiveness of hepatitis B vaccination.Objectives are to study the immune response to HBV vaccination and to correlate the antibody response with the duration of vaccination.

In this cross sectional study 150 medical interns were included. Single blood sample was drawn and anti HBs titration was done by chemiluminescence assay.Statistical analysis was done using SPSS for windows version 16.0.Vaccination rate was 94.6% and efficacy of vaccination was 88%. There was no association between gender and anti HBs titer (p value 0.13).Declining of anti HBs titer with duration of vaccination was significant (p=0.05).

As fall in anti HBs titer with the duration of the vaccination is an established fact, also considering Health care workers as the high risk population booster dose can be recommended to them.

Introduction:

Hepatitis B virus (HBV) infection is a major global public health problem. Of the approximately 2 billion people who have been infected worldwide, more than 350 million are chronic carriers of HBV[1]. India, with a carrier rate of 3%, contributes nearly 10% of the HBV carriers in the world [2].Every year over 1,00,000 Indians die due to illnesses related to HBV infection [3].

Since contact with body fluid of an infected person, especially infected blood,is one of the principal modes of transmission of the causative virus of Hepatitis B infection health care workers (HCW)constitute one of the high risk group for this infection[4].

Prevention of active infection by vaccination is an important strategy to decrease the risk of active HBV infection and of its subsequent complications. Antibody response to HBV surface antigen (Anti HBs)is an important serological marker for vaccine induced immunity to HBV.

It is a fact well documented that universal precautions are universally ignored. Medical students receive percutaneous injuries as often or more often than HCWs[5].

The issue concerning anti HBs level and the persistance of seroprotection are important in determing the potential need for the booster dose and there is a debate still exists on need of booster dose.

Hence this study was undertaken to assess the immune response of HBV vaccination among medical students and correlate the antibody response with the duration of vaccination.

Materials & Methods:

In this cross sectional study, 150 medical interns were included. 142 of them had completed the three doses of HBV vaccination and 8 of them had no vaccination. Informed consent was obtained from all the participants.

Using standard precautions 2ml of blood samples was drawn in a plain vacutainer from each participant and anti HBs titer was quantitatively measured by chemiluminescence assay

Basic demographic particulars and details regarding period of vaccination were collected and compiled.

Statistical Analysis:

Quantitative variables were expressed as mean with standard deviation and qualitative variables were expressed as numbers with percentage. Numerical data were calculated using Microsoft excel and analysed. Statistical analysis was done using SPSS for windows version 16.0.Data of samples were analysed by a chi square goodness of fit test. Difference between groups were assessed by a Students t-test. All two tailed p value of less than 0.05 were considered to be statistically significant.

Results:

The mean age of the participants was 22.There were 70 males and 80 females.

In this study a total of 150 individuals including 8 controls (non vaccinated individuals) were enrolled. Table [I] gives the components of the study population.

Table [II] consolidates the anti HBs titer among vaccinated and non vaccinated individuals .

The statistical difference between anti HBs titer of male and female is given is table [III].

Based on the measurement of their anti HBs titer the population was categorized into 3 groups non responder(less than 10 IU/L,hypo responders 10-100 IU/L)good responders (greater than 100 IU/L).The results were summerised in the Table [IV].

The period of vaccination was categorized into 4 groups, 0-6 months,7-12months, 1-5 years and >5years.The maximum samples were collected from the range 1-5years and minimum samples were collected from the range 7-12months.

The correlation of different period of vaccination with corresponding anti HBs titer is enumerated in table [V].

The statistical difference between anti HBs titer with period of vaccination is given is table[VI].

Discussion:

India has intermediate endemicity of hepatitis B with HBs Ag prevalance of 2-7% among population studied [6].

In 1991, The WHO recommended that hepatitis B vaccination should be included in national immunization system in all countries with a hepatitis B carrier prevalance (HBsAg) of 8% or greater by 1995 and in all countries by 1997.

Hepatitis B vaccine was introduced in Universal immunization programme of 10 states of India in the year 2007-2008[7].

The most important approach for the prevention of occupational HBV infection is the use of hepatitis B vaccine among HCW at risk.

In this study out of 150 medical interns 142 were vaccinated for HBV.Vaccination rate was 94.6%.8 of them were not vaccinated and they were included in the study as controls.

However, a study from Orissa in 2000 found that the vaccination rate was 86.7% among dental students and 79.5% among medical students[8].

In a study conducted at Iran although 86.8% of the health care workers had been vaccinated against hepatitis B, complete vaccination had been performed in only 71.7% of them[9].

We considered subjects as seropositive against hepatitis B if their anti HBs antibody concentration was greater than or equal to 10 IU/L and seronegative if it was less than 10 IU/L as recommended by the United States Advisory Committee on Immunization Practices and the World Health Organization (WHO) [10]

Of the 142 HBV vaccinated subjects,125 (88%)had anti HBs titer >10 IU/L and 17(12%)had anti HBs titer<10 IU/L.

In a 30 year follow up study conducted by Giuseppe Grosso out of the 292 anti-HBs positive HCWs, 261 HCWs had detectable anti-HBs titers, indicating a persistence of seroprotection of 89%[11].

Both plasma-derived hepatitis B vaccine and yeast-derived hepatitis B vaccine contain small surface protein of HBV and administration of these vaccines induces antibody to hepatitis B surface antigen (anti HBs) in more than 90% of HBV-uninfected, healthy normal individuals.[12] However, these vaccines are unable to induce protective levels of anti-HBs (10 IU/L) in about 5-10% of apparently healthy subjects.[13]

It is a fact that 5-10% of the adult population will not respond to standard HBV vaccination.[14]

Unresponsiveness to HB vaccine has been attributed to a number of environmental and genetic factors, the most important ones being the haplotype of HLA antigen and immunological tolerance[15].A variety of HLA class 1&2 antigens have been reported to be associated with unresponsiveness to the vaccine in different ethnic populations.[16]

Of the 8 non vaccinated controls,3(37.5%) had protective antibody response. This is similar to the study by G.Singh et al [17]. Due to subclinical infection and exposure 3 person might had developed anti HBs antibody.This needs further workup for the confirmation.

The average anti-HBs titer found among the male (561.7 IU/L) and female (665.33 IU/L) revealed no co-relation between the immunological memory and sex. P value was 0.13.[18]

Regarding immune response developed among vaccinated individuals, 72.5% and 15.4% were good-responders and hypo-responders respectively (Table IV).In a study by Bidhan Chakraborty 63.06% and 36.94% were good-responders and hypo-responders [19].

The geometric mean of serum anti HBs, for the post vaccination duration of 0-6months, 7-12months,1-5 years and >5 years is 562, 1000,652 and 419 respectively. The decrease in the mean of anti HBs titer with the duration of vaccination is significant. P value is 0.05,one way Anova F=2.74.

For the period < 1years of post vaccination, 83% were good responders, for the period of 1-5years and > 5years 73.6% and 60% were good responders. Declining of anti HBs titers with time after the primary vaccination is significant. P value is 0.05, X^2=9.38

The persistence of anti HBs depends on the peak antibody level achieved after three doses. In a study Kaplan- Maier survival curve of time from primary vaccination to an anti HBs antibody measurement outcome <10 IU/L, revealed that low post immunization titers (10- 99 IU/L)was a predictor of antibody loss during the follow-up period[11].

It is not uncommon to see anti HBs levels decline to low or undetectable levels during follow-up. In a follow-up study conducted in Taiwan,where HBV was highly endemic, the overall seropositive rate of anti HBs dropped from 99% at 1 Year of age to 83% at 5years of age[20].

All HCW should have serological testing 1-2 months following the final dose of the hepatities B vaccine.If adequate level is not achieved workup for occult HBV infection should be undertaken and revaccination should be considered.

Current data show that vaccine induced anti HBs level may decline over time, however, immune memory(anamnestic anti HBs response) remains intacts indefinitely following immunization[21].A few studies on the effect of HBV booster vaccinations have been done. At the end of the 9-12 years period of follow-up anti HBs were detected in 81% of children who received a booster dose at school age and in 68% of those who did not[22].

Though person with declining antibody levels are still protected against clinical illness and chronic disease local HBV endemicity should be taken into account when considering booster vaccination for HBV. High endemicity, such as that in most Asian countries, results in an increased risk of getting infected by the virus. With this concern, the steering committee for the prevention and control of infectious diseases in Asia has made a more conservative recommendation that whether to boost 10 years after primary vaccination should be judged by physicians on a case-by- case basis[23].

Conclusion:

Efficacy for HB vaccination has been well established. Booster vaccination, especially for vacinees who have lost their anti HBs should be considered, to enhance immune memory and provide reassurance of protective immunity against breakthrough infection, among medical interns. However more studies are necessary to highlight the need and timing of booster vaccination among HCWs.

Ideally, one should receive a complete course of HB vaccination, that is at least 3 doses. After that it is advisable to perform anti HBs assay to make sure that the response to vaccination was adequate or in other words to confirm whether the antibody titer was greater or equal to 10 IU/L .

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Table[I] Details of study population.n=150

Duration of vaccination	Number of participants
0-6 mths	8
7-12mths	4
1-5yrs	110
>5yrs	20
Non vaccinated	8

Table[II] Anti HBs antibody titer among vaccinated and nonvaccinated individuals.n=150

Study population	Anti HBs antibody titer		Total
	Protective >10 IU/L	Non protective <10 IU/L	
Vaccinated	125	17	142
Non vaccinated	3	5	8

Table[III]Statistical Difference between anti HBs titer of male and female participants.n=150

Sex	Number	Mean	SD	t-test	P value
Male	70	561.17	428.88	1.47	0.13
Female	80	665.33	429.55		

Table[IV]Distribution of good, hypo and non responders among vaccinated study population.n=142

Population	Anti HBs antibody titer (IU/L)	Status
103(72.5%)	>100	Good responders
22(15.4%)	10-100	Hypo responders
17(12%)	<10	Non responders

Table [V] Correlation of Anti HBs titer with duration of the vaccination.n=142

Duration	Non Responder	Hypo Responder	Good Responder
0-12 months(12)	-	2(16.6%)	10(83%)
1-5 years(110)	16(14.5%)	13 (12%)	81(73.6%)
75 years(20)	1(5%)	7(35%)	12(60%)

x2 =9.38 p=0.05

Table [VI] Statistical Difference between anti HBs titer and duration of vaccination

Duration of vaccination	Mean	SD	Number
0-6moths	562.05	429.26	8
7-12moths	1000	430.42	4
1-5yrs	652.81	430.4	110
more than 5yrs	419.2	429.54	20

One way Anova F=2.74 p=0.05

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